

471, 2006; M. D. Costa et al., “Dynamical glucometry: use of multiscale entropy analysis in diabetes,” *Chaos*, 24(3): 033139, 2014; [28]) that can report, in real-time, on salient aspects of integrative, multiscale, regulatory systems and of their breakdown with aging and disease. The use of these probes may enhance the clinical utility of traditional risk assessment tools (FIG. 19 and FIG. 20) and of other emerging technologies, such as genomic profiling. In furtherance of the goals of precision medicine, the dynamical property of HRF may also constitute a novel target for therapeutic interventions.

CONCLUSION

[0265] Analysis of short-term HRV is enhanced by a set of computational tools that quantify the fragmentation of heart-beat variability, defined by abrupt changes in the sign of HR acceleration. For example, heart rate fragmentation (HRF) is a manifestation of anomalous short-term sino-atrial variability. In a Holter monitor database from healthy subjects, the degree of fragmentation increased with the participants’ age. In particular, HRF was associated with increased risk of cardiac adverse events and cardiac mortality in MESA. Furthermore, fragmentation measures outperformed traditional short-term measures of HRV in discriminating a group of patients with CAD and from the healthy subjects. Fragmentation of sinus rhythm cadence may support a new class of dynamical biomarkers that probe the integrity of the regulatory network comprising neuroautonomic, sinus node and atrial components.

[0266] FIGS. 1-24 as described herein are illustrative examples allowing an explanation of the present invention. It should be understood that embodiments of the present invention could be implemented in hardware, firmware, software, or a combination thereof. In such an embodiment, the various components and steps would be implemented in hardware, firmware, and/or software to perform the functions of the present invention. That is, the same piece of hardware, firmware, or module of software could perform one or more of the illustrated blocks (i.e., components or steps).

[0267] The present invention can be implemented in one or more computer systems capable of carrying out the functionality described herein. Referring to FIG. 25, an example computer system 2500 useful in implementing the present invention is shown. Various embodiments of the invention are described in terms of this example computer system 2500. After reading this description, it will become apparent to one skilled in the relevant art(s) how to implement the invention using other computer systems and/or computer architectures.

[0268] The computer system 2500 includes one or more processors, such as processor 2504. The processor 2504 is connected to a communication infrastructure 2506 (e.g., a communications bus, crossover bar, or network).

[0269] Computer system 2500 can include a display interface 2502 that forwards graphics, text, and other data from the communication infrastructure 2506 (or from a frame buffer not shown) for display on the display unit 2530.

[0270] Computer system 2500 also includes a main memory 2508, preferably random access memory (RAM), and can also include a secondary memory 2510. The secondary memory 2510 can include, for example, a hard disk drive 2512 and/or a removable storage drive 2514, representing a floppy disk drive, a magnetic tape drive, an optical

disk drive, etc. The removable storage drive 2514 reads from and/or writes to a removable storage unit 2518 in a well-known manner. Removable storage unit 2518, represents a floppy disk, magnetic tape, optical disk, etc. which is read by and written to removable storage drive 2514. As will be appreciated, the removable storage unit 2518 includes a computer usable storage medium having stored therein computer software (e.g., programs or other instructions) and/or data.

[0271] In alternative embodiments, secondary memory 2510 can include other similar means for allowing computer software and/or data to be loaded into computer system 2500. Such means can include, for example, a removable storage unit 2522 and an interface 2520. Examples of such can include a program cartridge and cartridge interface (such as that found in video game devices), a removable memory chip (such as an EPROM, or PROM) and associated socket, and other removable storage units 2522 and interfaces 2520 which allow software and data to be transferred from the removable storage unit 2522 to computer system 2500.

[0272] Computer system 2500 can also include a communications interface 2524. Communications interface 2524 allows software and data to be transferred between computer system 2500 and external devices. Examples of communications interface 2524 can include a modem, a network interface (such as an Ethernet card), a communications port, a PCMCIA slot and card, etc. Software and data transferred via communications interface 2524 are in the form of signals 2528 which can be electronic, electromagnetic, optical, or other signals capable of being received by communications interface 2524. These signals 2528 are provided to communications interface 2524 via a communications path (i.e., channel) 2526. Communications path 2526 carries signals 2528 and can be implemented using wire or cable, fiber optics, a phone line, a cellular phone link, an RF link, free-space optics, and/or other communications channels.

[0273] In this document, the terms “computer program medium” and “computer usable medium” are used to generally refer to media such as removable storage unit 2518, removable storage unit 2522, a hard disk installed in hard disk drive 2512, and signals 2528. These computer program products are means for providing software to computer system 2500. The invention is directed to such computer program products.

[0274] Computer programs (also called computer control logic or computer readable program code) are stored in main memory 2508 and/or secondary memory 2510. Computer programs can also be received via communications interface 2524. Such computer programs, when executed, enable the computer system 2500 to implement the present invention as discussed herein. In particular, the computer programs, when executed, enable the processor 2504 to implement the processes of the present invention described above. Accordingly, such computer programs represent controllers of the computer system 2500.

[0275] In an embodiment where the invention is implemented using software, the software can be stored in a computer program product and loaded into computer system 2500 using removable storage drive 2514, hard disk drive 2512, interface 2520, or communications interface 2524. The control logic (software), when executed by the processor 2504, causes the processor 2504 to perform the functions of the invention as described herein.